

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Multiple sheets used when necessary)

SHEET 1 OF 3

Application No.	10/692,072
Filing Date	October 22, 2003
First Named Inventor	Botstein, et al.
Art Unit	1637
Examiner	Fredman, J.
Attorney Docket No.	GNE.2930R1C10C1

**U.S. PATENT DOCUMENTS**

Examiner Initials	Cite No.	Document Number Number - Kind Code (if known) Example: 1,234,567 B1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear
✓	1	6,025,156	02-15-2000	Gwynn, et al.	
	2	6,124,433	09-26-2000	Falb, et al.	
	3	6,156,500	12-05-2000	Falb, Dean	
	4	6,162,604	12-19-2000	Jacob, Chaim O.	
	5	6,228,582	05-08-2001	Rodier, et al.	
	6	6,395,306	05-28-2002	Cui, et al.	
	7	6,414,117	07-02-2002	Levinson, D. A.	
	8	6,465,185	10-15-2002	Goldfine, et al.	
	9	6,498,235	12-24-2002	Sheppard, et al.	
	10	6,562,343	05-13-2003	Levinson, D. A.	
	11	6,645,499	11-11-2003	Lal, et al.	
✓	12	6,730,502	05-04-2004	Van Hijum, et al.	
✓	13	6,737,522	05-18-2004	Sundick, et al.	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials	Cite No.	Foreign Patent Document Country Code-Number-Kind Code Example: JP 1234567 A1	Publication Date MM-DD-YYYY	Name of Patentee or Applicant	Pages, Columns, Lines Where Relevant Passages or Relevant Figures Appear	T <sup>1</sup>
✓	14	WO 97/38085	10-16-1997	California Pacific Medical Center		

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
✓	15	ALBERTS, et al. 1994. <i>Molecular Biology of the Cell</i> , 3rd Edition, pp. 403-404, 453. New York: Garland Publishing.	
	16	ALBERTS, et al. 2002. <i>Molecular Biology of the Cell</i> 4th Edition, pp. 302, 363-364, 379, 435. New York: Garland Publishing.	
✓	17	ALITALO 1984. Amplification of cellular oncogenes in cancer cells. <i>Med. Biol.</i> , 62:304-317	
✓	18	BANHASSY, et al. 2004. Cyclin A and cyclin D1 as significant prognostic markers in colorectal cancer patients. <i>BMC Gastroenterology</i> , 4:22-34.	

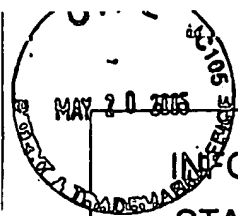
Examiner Signature

Date Considered

3/23/06

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.



PTO/SB/08 Equivalent

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Multiple sheets used when necessary)	Application No.	10/692,072
	Filing Date	October 22, 2003
	First Named Inventor	Botstein, et al.
	Art Unit	1637
SHEET 2 OF 3	Examiner	Fredman, J.
	Attorney Docket No.	GNE.2930R1C10C1

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
N	19	BIECHE, et al. 1998. Novel Approach to Quantitative Polymerase Chain Reaction Using Real-Time Detection: Application to the Detection of Gene Amplification in Breast Cancer. <i>Int. J. Cancer</i> . 78:661-666.	
	20	BLANCATO, et al. 2004. Correlation of amplification and overexpression of the c-myc oncogene in high-grade breast cancer: FISH, <i>in situ</i> hybridization and immunohistochemical analyses. <i>British Journal of Cancer</i> , 90(8), 1612-1619.	
	21	GRIMALDI, et al. 1989. The t(5;14) chromosomal translocation in a case of acute lymphocytic leukemia joins the interleukin-3 gene to the immunoglobulin heavy chain gene. <i>Blood</i> , 73(8):2081-2085.	
	22	GYGI, et al. Mar. 1999. Correlation between Protein and mRNA Abundance in Yeast. <i>Molecular and Cellular Biology</i> , 1720-1730.	
	23	HANNA, et al. Aug. 1999. HER-2/neu breast cancer predictive testing. <i>Pathology Associates Medical Laboratories</i> .	
	24	HEID, et al. 1996. Real Time Quantitative PCR. <i>Genome Res</i> . 6:986-994.	
	25	HIGUCHI, et al. April 1992. Simultaneous Amplification and Detection of Specific DNA Sequences. <i>Biotechnology</i> , 10:413-417.	
	26	HYMAN et al. Nov. 2002. Impact of DNA Amplification of Gene Expression Patterns. <i>Cancer Research</i> , 62:6240-6245.	
	27	LEWIN, B. 1994. Oncogenes: Gene Expression and Cancer, Chap. 39, pp.1196-1201. <i>Genes V</i> . New York: Oxford University Press.	
	28	LEWIN, B. 1997. Regulation of Transcription, Chap. 29, pp. 847-848. <i>Genes VI</i> . New York: Oxford University Press.	
	29	LIVAK, et al. 1995. Oligonucleotides with Fluorescent Dyes at Opposite Ends Provide a Quenched Probe System Useful for Detecting PCR Product and Nucleic Acid Hybridization. <i>PCR Methods Appl</i> 4:357-362.	
	30	MEEKER, et al. 1990. Activation of the interleukin-3 gene by chromosome translocation in acute lymphocytic leukemia with eosinophilia. <i>Blood</i> , 76(2):285-289.	
	31	MERIC, et al. 2002. Translation initiation in cancer: A novel target for therapy. <i>Molecular Cancer Therapeutics</i> , 1:971-979.	
	32	MERLINO, et al. 1985. Elevated Epidermal Growth Factor Receptor Gene Copy Number and Expression in a Squamous Carcinoma Cell Line. <i>J. Clin. Invest.</i> , 75:1077-1079	
	33	ØRNTOF, et al. 2002. Genome-wide study of gene copy numbers, transcripts, and protein levels in pairs of non-invasive and invasive human transitional cell carcinomas. <i>Molecular &amp; Cellular Proteomics</i> , 1:37-45.	
	34	PENNICA, et al. 1998. WISP genes are members of the connective tissue growth factor family that are up-regulated in Wnt-1 transformed cells and aberrantly expressed in human colon tumors. <i>Proc. Natl. Acad. Sci. USA</i> . 95(25):14717-14722.	
N	35	PITTI, et al., 1998. Genomic amplification of a decoy receptor for Fas ligand in lung and colon cancer. <i>Nature</i> . 396(6712):699-703.	

Examiner Signature	Date Considered 8/23/04
*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.	

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Multiple sheets used when necessary)

SHEET 3 OF 3

Application No.	10/692,072
Filing Date	October 22, 2003
First Named Inventor	Botstein, et al.
Art Unit	1637
Examiner	Fredman, J.
Attorney Docket No.	GNE.2930R1C10C1

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>1</sup>
<i>N</i>	36	POLLACK, et al. 2002. Microarray analysis reveals a major direct role of DNA copy number alteration in the transcriptional program of human breast tumors. <i>PNAS</i> , 99(20):12963-12968.	
<i>N</i>	37	SINGLETON, et al. 1992. Clinical and pathologic significance of the <i>c-erbB-2</i> ( <i>HER-2/neu</i> ) oncogene. <i>Pathol. Annu</i> , 1(27):165-190.	
<i>N</i>	38	ZHIGANG, et al. 2004. Prostate stem cell antigen (PSCA) expression in human prostate cancer tissues and its potential role in prostate carcinogenesis and progression of prostate cancer. <i>World Journal of Surgical Oncology</i> , 2:13.	

1717838  
051805

Examiner Signature

Date Considered

3/23/04

\*Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

T<sup>1</sup> - Place a check mark in this area when an English language Translation is attached.

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. GNE.2930R1C10	APPLICATION NO. 10/033,167
INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (USE SEVERAL SHEETS IF NECESSARY)		APPLICANT Botstein et al.	
		FILING DATE December 27, 2001	GROUP 1656



























U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE (IF APPROPRIATE)
<i>[initials]</i>	1.	5,536,637	07/16/96	Jacobs			
<i>[initials]</i>							


FOREIGN PATENT DOCUMENTS								
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)	
<i>[initials]</i>	2.	Akimaru et al. (1997) Drosophila CBP is a co-activator of cubitus interruptus in hedgehog signalling. Nature. 386:735-738.
<i>[initials]</i>	3.	Alcedo et al. (1996) The drosophila smoothened gene encodes a seven-pass membrane protein, a putative receptor for the hedgehog signal. Cell. 86:221-232.
<i>[initials]</i>	4.	Alexandre et al. (1996) Transcriptional activation of hedgehog target genes in drosophila is mediated directly by the cubitus interruptus protein, a member of the GLI family of zinc finger DNA-binding proteins. Genes & Development. 10:2003-2013.
<i>[initials]</i>	5.	Apelqvist et al. (1997) Sonic hedgehog directs specialised mesoderm differentiation in the intestine and pancreas. Current Biology. 7:801-804.
<i>[initials]</i>	6.	Bellusci et al. (1997) Involvement of sonic hedgehog (Shh) in mouse embryonic lung growth and morphogenesis. Development. 124:53-63.
<i>[initials]</i>	7.	Bitgood et al. (1996) Sertoli cell signaling by desert hedgehog regulates the male germline. Current Biology. 6(3):298-304.
<i>[initials]</i>	8.	Busson et al. (1988) Genetic analysis of viable and lethal fused mutants of drosophila melanogaster. Roux's Arch. Dev. Biol. 197:221-230.
<i>[initials]</i>	9.	Chen et al. (1996) Dual roles for patched in sequestering and transducing hedgehog. Cell. 87:553-563.
<i>[initials]</i>	10.	Chiang et al. (1996) Cyclopia and defective axial patterning in mice lacking sonic hedgehog gene function. Nature. 383:407-413.
<i>[initials]</i>	11.	Chidambaram et al. (1996) Mutations in the human homologue of the Drosophila patched gene in Caucasian and African-American nevoid basal cell carcinoma syndrome patients. Cancer Research. 56:4599-4601.
<i>[initials]</i>	12.	Dominguez et al. (1996) Sending and receiving the hedgehog signal: control by the drosophila Gli protein cubitus interruptus. Science. 272:1621-1625.
<i>[initials]</i>	13.	Echelard et al. (1993) Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity. Cell. 75:1417-1430.
<i>[initials]</i>	14.	Ericson et al. (1995) Sonic hedgehog induces the differentiation of ventral forebrain neurons: a common signal for ventral patterning within the neural tube. Cell. 81:747-758.
<i>[initials]</i>	15.	Fan and Tessler-Lavigne (1994) Patterning of mammalian somites by surface ectoderm and notochord: evidence for sclerotome induction by a hedgehog homolog. Cell. 79:1175-1186.
<i>[initials]</i>	16.	Gailani et al. (1996) The role of the human homologue of drosophila patched in sporadic basal cell carcinomas. Nature Genetics. 14:78-81.
<i>[initials]</i>	17.	Grau and Simpson (1987) The segment polarity gene costal-2 in drosophila. Developmental Biology. 122:188-200.
<i>[initials]</i>	18.	Hahn et al. (1996) Mutations of the human homolog of drosophila patched in the nevoid basal cell carcinoma syndrome. Cell. 85:841-851.
<i>[initials]</i>	19.	Hooper and Scott (1989) The drosophila patched gene encodes a putative membrane protein required for segmental patterning. Cell. 59:751-765.

EXAMINER	DATE CONSIDERED 3/23/00
*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.	

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. GNE.2930R1C10	APPLICATION NO. 10/033,167
INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (USE SEVERAL SHEETS IF NECESSARY)		APPLICANT Botstein et al.	
		FILING DATE December 27, 2001	GROUP 1656

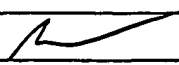
EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
	20. Hynes et al. (1995) Induction of midbrain dopaminergic neurons by sonic hedgehog. Neuron. 15:35-44.
	21. Hynes et al. (1997) Control of cell pattern in the neural tube by the zinc finger transcription factor and oncogene Gli-1. Neuron. 19:15-26.
	22. Ingham (1995) Signalling by hedgehog family proteins in drosophila and vertebrate development. Current Opinion in Genetics and Development. 5:492-498.
	23. Jiang and Struhl (1998) Regulation of the hedgehog and wingless signalling pathways by the F-box/WD40-repeat protein Slimb. Nature. 391:493-496.
	24. Johnson et al. (1994) Ectopic expression of sonic hedgehog alters dorsal-ventral patterning of somites. Cell. 79:1165-1173.
	25. Johnson et al. (1996) Human homolog of patched, a candidate gene for the basal cell nevus syndrome. Science. 272:1668-1671.
	26. Klein et al. (1996) Selection for genes encoding secreted proteins and receptors. Proc. Natl. Acad. Sci. USA. 93:7108-7113.
	27. Krauss et al. (1993) A functionally conserved homolog of the drosophila segment polarity gene hh is expressed in tissues with polarizing activity in zebrafish embryos. Cell. 75:1431-1444.
	28. Krishnan et al. (1997) Mediation of sonic hedgehog-induced expression of COUP-TFII by a protein phosphatase. Science. 278:1947-1950.
	29. Laufer et al. (1994) Sonic hedgehog and Fgf-4 act through a signaling cascade and feedback loop to integrate growth and patterning of the developing limb bud. Cell. 79:993-1003.
	30. Lee et al. (1997) Gli1 is a target of sonic hedgehog that induces ventral neural tube development. Development. 124:2537-2552.
	31. Mariño et al. (1996) Biochemical evidence that patched is the hedgehog receptor. Nature. 384:176-179.
	32. Marti et al. (1995) Requirement of 19K form of sonic hedgehog for induction of distinct ventral cell types in CNS explants. Nature. 375:322-325.
	33. Nakano et al. (1989) A protein with several possible membrane-spanning domains encoded by the drosophila segment polarity gene patched. Nature. 341:508-513.
	34. Nüsslein-Volhard et al. (1984) Mutations affecting the pattern of the larval cuticle in drosophila melanogaster. Roux's Arch. Dev. Biol. 193:267-282.
	35. Orenic et al. (1990) Cloning and characterization of the segment polarity gene cubitus interruptus dominant of drosophila. Genes & Development. 4:1053-1067.
	36. Oro et al. (1997) Basal cell carcinomas in mice overexpressing sonic hedgehog. Science. 276:817-821.
	37. Pemimon (1995) Hedgehog and beyond. Cell. 80:517-520.
	38. Pham et al. (1995) The suppressor of fused gene encodes a novel PEST protein involved in drosophila segment polarity establishment. Genetics. 140:587-598.
	39. Préal et al. (1990) A putative serine/threonine protein kinase encoded by the segment-polarity fused gene of drosophila. Nature. 347:87-89.
	40. Préal (1992) Characterization of suppressor of fused, a complete suppressor of the fused segment polarity gene of drosophila melanogaster. Genetics. 132:725-736.
	41. Préal et al. (1993) Segmental polarity in drosophila melanogaster: genetic dissection of fused in a suppressor of fused background reveals interaction with costal-2. Genetics. 135:1047-1062.
	42. Riddle et al. (1993) Sonic hedgehog mediates the polarizing activity of the ZPA. Cell. 75:1401-1416.
	43. Roberts et al. (1995) Sonic hedgehog is an endodermal signal inducing Bmp-4 and Hox genes during induction and regionalization of the chick hindgut. Development. 121:3163-3174.
	44. Robbins et al. (1997) Hedgehog elicits signal transduction by means of a large complex containing the kinesin-related protein costal2. Cell. 90:225-234.
	45. Roelink et al. (1995) Floor plate and motor neuron induction by different concentrations of the amino-terminal cleavage product of sonic hedgehog autoproteolysis. Cell. 81:445-455.
	46. Simpson and Grau (1987) The segment polarity gene costal-2 in drosophila. Developmental Biology. 122:201-209.
	47. Sisson et al. (1997) Costal2, a novel kinesin-related protein in the hedgehog signaling pathway. Cell. 90:235-245.

EXAMINER 	DATE CONSIDERED 3/23/01
*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.	

FORM PTO-1449	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO. GNE.2930R1C10	APPLICATION NO. 10/033,167
INFORMATION DISCLOSURE STATEMENT BY APPLICANT  (USE SEVERAL SHEETS IF NECESSARY)		APPLICANT Botstein et al.	
		FILING DATE December 27, 2001	GROUP 1656

EXAMINER INITIAL	OTHER DOCUMENTS (INCLUDING AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.)
✓	48. Stone et al. (1996) The tumour-suppressor gene patched encodes a candidate receptor for sonic hedgehog. Nature. 384:129-134.
	49. Thérond et al. (1996) Functional domains of fused, a serine-threonine kinase required for signaling in drosophila. Genetics. 142:1181-1198.
	50. Thérond et al. (1996) Phosphorylation of the fused protein kinase in response to signaling from hedgehog. Proc. Natl. Acad. Sci. USA. 93:4224-4228.
	51. Uden et al. (1996) Mutations in the human homologue of drosophila patched (PTCH) in basal cell carcinomas and the gortin syndrome: different in vivo mechanisms of PTCH inactivation. Cancer Research. 56:4562-4565.
	52. Van den Heuvel and Ingham (1996) Smoothed encodes a receptor-like serpentine protein required for hedgehog signalling. Nature. 382:547-551.
	53. Wicking et al. (1997) Most germ-line mutations in the nevoid basal cell carcinoma syndrome lead to a premature termination of the PATCHED protein, and no genotype-phenotype correlations are evident. Am. J. Hum. Genet. 60:21-26.
	54. Xie et al. (1998) Activating smoothed mutations in sporadic basal-cell carcinoma. Nature. 391:90-92.
✓	55. Database search, Locus list: hum (349, 801 seqs, 66, 964, 548 aa), Mon Jan 7 16:12:49 2002 [BLASTP 2.2.1 [Jul-12-2001], NCBI] 2 pp.
✓	56. Database search, Locus list: hum - est (1, 803, 435 seqs, 6, 559, 376, 613 bp), Tue Jan 8 09:15:52 2002 [BLASTN 2.2.1 [Jul-12-2001], NCBI] 8 pp

S:\DOCS\LD\LD-2239.DOC\051002

EXAMINER 	DATE CONSIDERED 3/23/02
*EXAMINER: INITIAL IF CITATION CONSIDERED, WHETHER OR NOT CITATION IS IN CONFORMANCE WITH MPEP 609; DRAW LINE THROUGH CITATION IF NOT IN CONFORMANCE AND NOT CONSIDERED, INCLUDE COPY OF THIS FORM WITH NEXT COMMUNICATION TO APPLICANT.	